

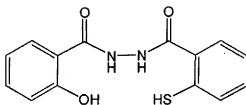
## REMARKS

Claims 1-115 are pending in this application; Claims 4-6, 10-12, and 15-115 having been withdrawn by the amendment of 12 June, 2006.

In the Office Action dated June 8, 2007, the Examiner withdrew all prior rejections with the exception of Janda, US 6,664,372 (hereinafter as "US '372). The Examiner rejected Claims 1-3 and objected to Claims 7-9 and 14 because of their dependence on the rejected Claims. The Examiner cites two new references, Zhao (J. Med. Chem. **40**, 937-941, 1997, hereinafter as "Zhao"), and Young, US 4,767,745 (hereinafter as "US '745").

### *Rejection under 35 U.S.C. 103(a)*

In the present Office Action, the Examiner rejected Claims 1 and 2 under 35 U.S.C. 103(a) as being unpatentable over Zhao, a single reference. According to the Examiner, Zhao discloses a compound having the structure:



that allegedly anticipates Claim 1 when Y is phenol, L is  $-\text{C}_6\text{H}_4-$  and Q is  $-\text{SH}$ .

To show obviousness, the reason or motivation offered by the prior art need not offer "absolute predictability" of the results, but it requires at least a "reasonable expectation of success." *Yamanouchi*, 231 F.3d 1339 at 1343 (Fed. Cir. 2000), quoting *In re Longi*, 759 F.2d 887, 896 (Fed. Cir. 1985); accord, *In re Vaec*, 947 F.2d 488, 495 (Fed. Cir. 1991) (reversing PTO rejection of claims as obvious where prior art offered no "reasonable expectation of success"), citing *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988). Obviousness cannot be determined by chemical structure alone. As applied to chemical compounds, "a compound and all of its properties are inseparable" and must be considered in determining obviousness. *In re Dillon*, 919 F.2d 688, at 697 (Fed. Cir. 1990), citing *In re Papesch*, 315 F.2d at 381, 137 USPQ 43 (CCPA 1963); accord, *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 725 (Fed. Cir. 1990) (affirming rejection of

obviousness defense: "An analysis of obviousness of a claimed combination must include consideration of the results achieved by that combination.").

Applicants respectfully note that in Claim 1 of the present application, Y is defined as "a residue of a macromolecule" wherein a macromolecule is defined in the present application as "any compound having at least one group that can react with a hydrazide compound ... oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, or a glycolipid ... a polysaccharide, a protein, or a synthetic polymer." See paragraph [0055] of Publication No. US 2005/0176620. The Examiner cites Zhao as a single reference, alleging that when Y is a phenol group in the above structure, the structure renders Claim 1 obvious because the phenol group corresponds to the "residue of a macromolecule" as recited in Claim 1.

Applicants respectfully traverse the rejection. First, one skilled in the art would not normally consider a phenol group as a macromolecule, as such phenol group or a similar compound would be typically considered to be a small molecule. Second, Claim 1, as presently amended, further clarifies the claims to define a macromolecule as an "... oligonucleotide, nucleic acid, polysaccharide, a protein, or a synthetic polymer," all macromolecules of which have significantly higher molecular weights than a phenol group. Applicants respectfully note that small molecules such as a phenol group have significantly different structure, chemical and physical properties than a macromolecule, and there is no reasonable expectation of success for providing a compound having the same properties by exchanging a phenol group in a compound for a macromolecule.

Applicants respectfully request the reconsideration and withdrawal of the rejection of Claim 1 in view of Zhao.

The Examiner rejected Claims 1 and 2 under 35 U.S.C. 103 as being unpatentable over US '745, also a single reference. According to the Examiner, US '745 discloses compound VIII at columns 7-8 (second to last structure) that is encompassed by Claim 1 when the variables of Claim 1 are: Y = leukotriene; L = polyalkylene and Q is maleimide.

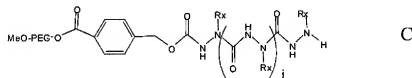
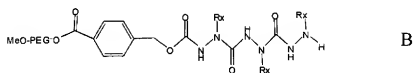
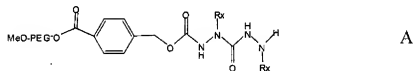
Applicants respectfully traverse the rejection. First, similar to the above reasoning, one skilled in the art would not normally consider a leukotriene group as a macromolecule, as such leukotriene group or a similar compound would be typically considered to be a small molecule. Second, Claim 1, as presently amended, further clarifies the claims to define a macromolecule as an "... oligonucleotide, nucleic acid, polysaccharide, a protein, or a synthetic polymer," all

macromolecules of which have significantly higher molecular weights than a leukotriene group. Applicants respectfully note that small molecules such as a leukotriene have significantly different structure, chemical and physical properties than a macromolecule, and there is no reasonable expectation of success for providing a compound having the same properties by exchanging a leukotriene in a compound for a macromolecule, as presently defined in Claim 1.

Applicants respectfully request the reconsideration and withdrawal of the rejection of Claims 1 and 2 in view of US '745.

On page 4 of the Office Action, the Examiner maintained the rejection Claims 1 and 3 under 35 U.S.C. 103 as being unpatentable over Janda (US '372), also a single reference. In the Response of March 27, 2007, Applicants asserted that

*Applicants note that the compounds disclosed in US '372, as referred to by the Examiner, are "oligoazatide compounds" (see column 4, line 49) because, where  $i$  is 0,  $i$  is 1 or where  $i$  is  $\leq 99$ , then the compound has the structure of either A, B or C below:*



*As apparent from the structures of the compounds shown above, where  $i$  is 0, 1 or  $\leq 99$ , the compounds disclosed in US '372 are dihydrazides, tri-hydrazides or poly-hydrazides. On the other hand, the compound recited in Claim 1, as presently amended, has the corresponding group "L-Q" wherein the group L-Q corresponds*

*to the explicitly listed functional groups, none of which are dihydrazides, tri-hydrazides or poly-hydrazides.*”

In the present Office Action, the Examiner asserts that Applicants’ response of March 27, 2007 argued “in effect that if one takes a macromolecule, and attaches a hydrazide group to it, or several hydrazide groups to it, the property of being a macromolecule is somehow lost. Or alternatively, that the term “Y” in instant claim 1 excludes hydrazide groups.” Applicants respectfully note that the Examiner mischaracterized Applicants’ response.

First, in reference to the group –L-Q the formula I, which corresponds to the group as disclosed in US '372 are dihydrazides, tri-hydrazides or poly-hydrazides, wherein the terminal nitrogen of the hydrazides is functionalized with the group  $R_x$  wherein “ $R_x$  is selected from the group consisting of hydrogen, methyl, isobutyl, isopropyl,  $C_1$ - $C_6$  alkyl, benzyl, substituted benzyl and the side chain radical of the following amino acids: Ala, Arg, Asn, Asp, Asx, Cys, Gln, Glu, Glx, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr and Val.” See column 4, lines 58-64. On the other hand, as recited in Claim 1, the group –L-Q are defined as

Q is a SH group, or is selected from the group consisting of  $C_{1-24}$  alkyl halide,  $C_{1-24}$  alkoxy- $C_{1-24}$  alkyl,  $\alpha$ -halocarbonyl, maleimides, vinyl sulfones, acrylonitriles,  $\alpha$ -methylene esters, quinine methides, acryloyl esters, acryloyl amide,  $\alpha$ -halo esters and  $\alpha$ -halo amides; and

L is a polyalkylene group, a polyether group, a polyamide group, a polyimino group, an aryl group, a polyester, or a polythioether group, ...

Applicants respectfully note that no possible combinations of the groups –L-Q, as defined in Claim 1, corresponds to the dihydrazides, tri-hydrazides or poly-hydrazides groups, wherein the terminal nitrogen of the hydrazide is functionalized with the group  $R_x$  because at least in part, no member of L, as defined above, corresponds to a hydrazide.

At the same time, on page 4 of the Office Action, the Examiner refers to the variable “Y” as recited in Claim 1, and note that Applicants’ arguments of March 27, 2007 is not correct because Applicants argued that “the term “Y” in instant claim 1 excludes hydrazide groups;” or that “if one takes a macromolecule, and attaches a hydrazide group to it, or several hydrazide groups to it, the property of being a macromolecule is somehow lost.” As noted above, Claim 1 recites a compound

containing a hydrazide group wherein the group –L-Q on one side (the right hand side of Formula I) of the hydrazide clearly do not define a hydrazide group.

And on the other side of the hydrazide compound of Formula I of Claim 1, the variable Y is specifically defined as “a residue of a macromolecule, wherein the macromolecule is a compound having at least one group that can react with a hydrazide compound, wherein the compound is selected from the group consisting of an oligonucleotide, a nucleic acid or a metabolically stabilized analogue thereof, a polypeptide, a lipid, a glycoprotein, a glycolipid, a polysaccharide, a protein, and a synthetic polymer ...” Applicants note that, while the definition for Y does not explicitly exclude the option or permutation that the macromolecule may be functionalized with a hydrazide, the definition for Y clearly does not recite that Y is a hydrazide that is attached to a macromolecule. Applicants note that the Examiner’s criticism of Applicants’ response (that Applicants never asserted) that when a hydrazide is attached to the macromolecule, “the property of being a macromolecule is somehow lost” is misplaced.

In view of the amendment to Claim 1, and therefore, to dependent Claim 2, and the clear distinctions between the compounds of the present Claim 1 and the disclosure of US '372 as noted above, Applicants respectfully assert that the present claims are not obvious in view of US '372. The Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 1 and 2 under 35 U.S.C. 103.

In view of the foregoing amendments and remarks, Applicant submits that all of the claims are in proper format and are patentably distinct from the prior art of record and are in condition for allowance. Applicants respectfully request withdrawal of the rejection of Claims 1, 2 and 3, and accordingly, dependent Claims 7-9, and 13-14 as being obvious under 35 U.S.C. 103.

**CONCLUSION**

Entry of the amendments, and reconsideration of the rejection of Claims 1, 2 and 3 and accordingly, dependent Claims 7-9, and 13-14 in view of the foregoing amendment and remarks, and allowance of the claims are respectfully requested.

If there are any issues remaining that the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the contact information listed below.

Date: November 8, 2007

Respectfully submitted,  
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